REMARKS/ARGUMENTS

Claim Status.

Claims 13-17 are pending. Applicants acknowledge with appreciation the withdrawal of prior rejections.

The claims stand rejected, either alone or in subsets, under 35 U.S.C. Section 102, Section 103, Section 112, second paragraph, and for double patenting.

Claims 13,16 and 17 have been amended to more particularly point out and distinctly claim that which Applicants consider to be the invention and to conform with helpful suggestions made by the Examiner. These amendments are discussed at length below and are fully supported in the specification as filed, thus, no new matter has been introduced.

Claim Objections

The claims have been objected to under 37 CFR 1.75(c). More specifically, the Office Action states that claims 16 and 17 are in improper dependent form for failing to further limit the subject matter of a previous claim from which they depend.

In response, claim 16 has been amended to recite a specific binding partner of APRIL or AGP-3, instead of a specific binding partner of BCMA or TACI. A specific binding partner of either of APRIL or AGP-3 is similar in scope to a composition comprising a region of TACI and BCMA as described in claim 14. This amendment is supported in the specification as filed on page 33, lines 16-18. In addition it is believed that the amendment overcomes the objection.

Rejection under Section 112, second paragraph.

Claims 13-17 are rejected as being indefinite. The Office Action states that claim 13 recites a composition comprising a 'vehicle,' and that the use of this term is repugnant to its usual meaning. The Examiner notes that amendment of the claims to change the definition of F^1 from 'vehicle' to the list of substances on page 13, line 20 to page 14, line 2 would obviate this rejection. In response, Applicants have so amended claim 13.

It is also noted that claims 13, 15, and 17 do not define 'L' in the formula. In response, claim 13 has been amended to define the various 'L' groups in the formula as linkers. Support for this amendment can be found in the specification as filed in the paragraph bridging pages 32 to 33. Omission of this definition was a clerical oversight and no new matter is added.

It is respectfully submitted that the above-made amendments overcome this rejection.

Rejection under Section 102.

Claim 16 is rejected as anticipated in view of Tschopp (WO 99/12965). Tschopp teaches APRIL nucleic acids and proteins, and specifically teaches an APRIL polypeptide, such as the extracellular domain, fused to a marker or tagging sequence.

As discussed above, claim 16 has been amended so that it recites a specific binding partner of APRIL and/or AGP-3. In addition, claim 13 has been amended to provide a definition for the 'L' moiety in the molecule claimed clarifying the scope of claim 16, and proving the Examiner's original assumptions were correct. Accordingly, since Tschopp does not teach a specific binding partner of AGP-3 or APRIL such as a consensus sequence of TACI, a consensus sequence of BCMA, or a TACI/BCMA extracellular consensus sequence fused to another peptide sequence as presently claimed, it is submitted that the amended claims are not anticipated by Tschopp and withdrawal of this rejection is respectfully requested.

First Rejection under Section 103.

Claims 13-15 are rejected as unpatentable over Gross et al., (Nature, 2000, 404:995-999), in view of Tschopp and Naismith et al. (Structure, 1996, 4:1251-1262). Gross et al. teach TACI-Ig and BCMA-Ig fusion proteins and that these fusions affect ZTNF4 activity on immune cells, where Ig represents the Fc portion of an immunoglobulin. Gross et al. further suggest that these fusions may be useful to treat autoimmune diseases. Tschopp teaches that the cysteine rich extracellular domains of the TNF receptor family is a ligand binding domain. Naismith et al. teach motifs within tumor necrosis factor receptors that identify the cysteine rich motif. It is acknowledged that Gross et al., Tschopp, and Naismith et al. each individually do not teach identifying a consensus motif, or the fusion of a consensus sequence to a 'vehicle' such as an Fc domain of an immunoglobulin as taught by the Applicants.

It is specifically alleged that it would have been *prima facia* obvious by one of ordinary skill in the art to combine the teachings of the three references to arrive at the claimed invention, where motivation to do so comes from the desire to suppress B-cell mediated autoimmune disorders such as lupus.

Applicants respectfully disagree for the following reasons. When developing a protein therapeutic, it is typical that the scientists would choose to focus on a sequence that has the desired function, *e.g.,* B cell activation inhibition. Just as typically, the first sequence that would be tested would likely be a natural sequence identified from proteins domains from known proteins from cDNA libraries or the like, such as was done with TACI and BCMA. In other words, native protein sequences. Once the desired function is demonstrated there is no motivation to change that sequence or to develop alternatives since a working therapeutic has been identified.

It could be argued that if there were a negative side effect by that natural sequence, and it could be overcome by making changes to the sequence, then there would possibly be motivation for developing alternatives

but here there is no such teaching in the cited references. And since Gross et al. described successfully blocking signaling and B cell activation with native sequences *in vitro* with no obvious negative side effects, there is no motivation to proceed as Applicants have.

Also in a practical sense, and rhetorically speaking, why should one try to get an alternative sequence to a successful therapeutic, such as a consensus sequence, when one already has a native sequence that works? This would simply create additional work for the scientists without obvious benefit. In order for there to be proper motivation, the art must teach some kind of additional benefit beyond using the native sequence TACI or BCMA fusions and the cited art does not do so.

Thus, it is respectfully submitted that there is no motivation to combine the cited references as described in the Office Action to obtain a consensus sequence because useful native proteins have already been described. In addition, there were no known problems or side effects with using the native sequence at the time of the references so there was no motivation arose to make a consensus sequence to avoid those problems. Accordingly, it is respectfully submitted that a *prima facia* case for obviousness has not been made and withdrawal of this rejection is requested.

Second Rejection under Section 103.

Claims 16 and 17 are rejected as unpatentable over Tschopp in view of Ward (WO97/34631). Tschopp teaches APRIL proteins and fusions of APRIL with markers. Ward teaches that fusion of proteins to Fc domains can stabilize and/or increase the longevity of the protein for therapeutic or diagnostic uses. Thus it is alleged that it would have been obvious to combine the teachings of Tschopp and Ward to arrive at the invention of claims 16 and 17.

As noted above, claim 16 has been amended to recite a specific binding partner of AGP-3 or APRIL instead of TACI or BCMA. Thus, the presently claimed invention no longer recites molecules that could encompass APRIL or APRIL-like molecules either alone or fused to a 'vehicle' such as an Fc domain. Accordingly, it is believed that this rejection is now mooted and withdrawal is requested.

Double Patenting.

Claims 16 and 17 have also been provisionally rejected under the judicially created doctrine of double patenting in view of claims 27-30 of co-pending Application No. 09/854,864 as drawn to specific binding partners of TACI and BCMA. Claim 16 has been amended to recite a specific binding partner of AGP-3 and/or APRIL and no longer recites subject matter that is commensurate in scope with the co-pending claims. Accordingly, it is believed that this rejection is mooted by the amendment and withdrawal is requested.

Conclusion.

In light of the foregoing amendments and remarks, the Applicants respectfully request entry of all amendments, withdrawal of all rejections and objections, and allowance of all claims.

Respectfully submitted,

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